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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09 462,846	01 13 2000	DAVID A. ESTELL	GC381-US	5580

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GENENCOR INTERNATIONAL, INC.
ATTENTION: LEGAL DEPARTMENT
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EXAMINER

STEADMAN, DAVID J

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 05-16-2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/462,846

Applicant(s)

ESTELL, DAVID A.

Examiner

David J. Steadman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 March 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 6-13, 15 and 20-23 is/are pending in the application.
- 4a) Of the above claim(s) 2, 3, 10-12, 22 and 23 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1 and 6-9 is/are allowed.
- 6) ☒ Claim(s) 13, 15, 20 and 21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 15. 6) ☐ Other: _____

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DETAILED ACTION

Application Status

- [1] Claims 1-3, 6-13, 15, and 20-23 are pending in the application.
- [2] Applicant's amendment to the specification and claims 6-9, 13, 15, and 20 in Paper No. 23, filed March 12, 2003, is acknowledged.
- [3] Claims 2, 3, 10-12, 22, and 23 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim.
- [4] Claims 1, 6-9, 13, 15, 20, and 21 are being examined on the merits.
- [5] Applicants' arguments filed in Paper No. 23 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.
- [6] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.
- [7] It is noted that applicants state in Paper No. 17 that references cited on Form PTO-1449 but not filed with the Information Disclosure Statement will not be submitted as requested by the examiner. Therefore, these references have not been considered and a signed and dated copy of Form PTO-1449 is attached to the instant Office action.

Claim Objections

- [8] Claims 13 and 20 are objected to in the recitation of "cysteine protease 1" as using inconsistent terminology. As claims 1, 22, and 23 recite "cysteine protease-1", it is suggested that applicant maintain consistent use of terminology throughout the claims and replace "cysteine protease 1" in claims 13 and 20 with "cysteine protease-1".

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Claim Rejections - 35 USC § 112, Second Paragraph

[9] Claims 13, 15, 20, and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 (claims 15, 20, and 21 dependent therefrom) is confusing in that it is unclear as to whether the mutation or deletion in the gene encoding *B. subtilis* CP1 results in the inactivation of CP1, or if CP1 is inactivated by some other mechanism. One of skill in the art recognizes that, while mutation or deletion of an encoding nucleic acid can result in the inactivation of an enzyme, enzymes can be inactivated in other ways as well such as chemical inhibition of enzymatic activity. In order to clarify the meaning of the claim, it is suggested that, for example, part (a) of claim 13 be amended as follows: "obtaining a *Bacillus subtilis* host cell comprising a nucleic acid encoding said heterologous protein wherein said host cell contains a mutation or deletion in the gene encoding *B. subtilis* cysteine protease-1, wherein said gene encoding cysteine protease-1 encodes the amino acid sequence set forth in SEQ ID NO:2 and said mutation or deletion results in the inactivation of the cysteine protease-1 proteolytic activity; and".

Claim Rejections - 35 USC § 112, First Paragraph

[10] The written description rejection of claims 15 and 21 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a previous Office action (see item 5 of Paper No. 22). Addressing mutants of apr, npr, epr, wpr, and mpr proteases, applicant argues (pages 5 and 6 of Paper No. 23) the specification cites publications that describe mutations of these proteases. Applicant argues that, as these mutants are known in the art, there is no requirement that applicant provide a detailed description of the claimed embodiments. Applicant's argument is not found persuasive. It is noted the specification states that the cited publications describe *B. subtilis* host cells with deletions of the recited proteases. It is acknowledged that *B. subtilis* host cells with deletions of the recited proteases are known in the art as evidenced by the

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specification's citation of publications describing such *B. subtilis* host cells (page 9, lines 5-10 of the instant specification). However, the claims encompass a genus of mutant apr, npr, epr, wpr, and mpr proteases having any function including increased protease activity, decreased protease activity, no protease activity, or other, undescribed enzymatic activities. One of skill in the art would recognize that the genus of recited mutant apr, npr, epr, wpr, and mpr proteases is widely variant and each of the proteases can have any function. In an unpredictable art, adequate written description of a genus that embraces widely variant species cannot be achieved by disclosing only one species within the genus. As such, the specification fails to describe relevant identifying characteristics of a representative number of species of the genus of mutant proteases sufficient to show possession.

[11] The scope of enablement rejection of claims 15 and 21 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a previous Office action (see item 6 of Paper No. 22). Addressing mutants of apr, npr, epr, wpr, and mpr proteases, applicant argues (pages 6 and 7 of Paper No. 23) there is no requirement to disclose all mutations that result in inactivation. Applicant argues there the specification is enabling for mutations in other proteases. Applicant's argument is not found persuasive. It is noted that the claims are not so limited to mutations of apr, npr, epr, wpr, and mpr proteases that result in their inactivation. As written, the claims are so broad as to encompass mutant apr, npr, epr, wpr, and mpr proteases having *any* activity. The specification fails to provide guidance or working examples to enable mutant apr, npr, epr, wpr, and mpr proteases having any activity. Because the specification fails to provide guidance and working examples to enable the entire scope of mutant apr, npr, epr, wpr, and mpr proteases, a high degree of unpredictability exists in making and using the entire scope of *Bacillus subtilis* host cells as recited in the claims. As stated in a previous Office action, while recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within an encoded protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is

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unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. The prior art teaches that modifications to an encoding nucleic acid, even minor modifications, may completely alter the function of the encoded protein sequence. As a representative example, Broun et al. (*Science* 282:1315-1317, 1998) teach that as few as four amino acid substitutions in a polypeptide having approximately 380 amino acids completely alters the enzymatic function of the polypeptide from a desaturase to a hydroxylase (see abstract). Thus, without sufficient guidance, there is a high degree of unpredictability in mutating an encoding nucleic acid with an expectation of obtaining a polypeptide having the desired function. Due to the broad scope of mutant apr, npr, epr, wpr, and mpr proteases, the lack of guidance and working examples, and the high degree of unpredictability in mutating a sequence with an expectation of obtaining a protein with a desired activity, undue experimentation would be required. Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

Conclusion

- [12]** Claims 1-3, 6-13, 15, and 20-23 are pending.
- [13]** Claims 1 and 6-9 are in condition for allowance.
- [14]** Claims 13, 15, 20, and 21 are rejected.
- [15]** Claims 13, 15, 20, and 21 would be allowable if rewritten to overcome the objection(s) and/or rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action.
- [16]** Claims 2, 3, 10-12, 22, and 23 are withdrawn from consideration.

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Applicant's amendment to claim 13 necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Thursday from 6:30 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for this Group is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.
Patent Examiner
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[Handwritten signature]
David J. Steadman